

Appl. No. 10/668,778  
Amdt. dated October 29, 2007  
Amendment under 37 CFR 1.116 Expedited Procedure  
Examining Group 1639

PATENT

## REMARKS/ARGUMENTS

### **I. INTERVIEW**

We acknowledge and thank Examiner Gross and Examiner Epperson for the phone interview on October 17, 2007, to discuss the status of the case, the outstanding rejections, and proposed claim amendments. No agreement was reached during the interview. The claim amendments and arguments presented herein are consistent with the discussions during the phone interview.

### **II. STATUS OF THE CLAIMS**

With entry of this amendment, claims 1-62, 65 and 67 are canceled, and claims 64, and 68-70 are withdrawn as being directed to non-elected embodiments. Claims 63, 66, 72 and 74 are currently amended and claims 75-77 are newly added. Claims 63, 66, and 71-77 are currently being examined. No new matter is added.

### **III. SUPPORT FOR THE CLAIM AMENDMENTS**

Support for the claim amendments can be found throughout the application as filed, as well as U.S. Pat. App. No 09/526,106, ('106 app.) filed March 15, 2000, of which the present application is a continuation, and U.S. Prov. App. No. 60/124339 ('339 app.) filed March 19, 1999, of which the instant application claims priority.

Specifically, Claim 63 is amended to clarify that the N-terminal and the C-terminal fragment are not less than 25 amino acids in length. Support for this amendment can be found throughout the application as filed, for Example, at page 6, paragraph [0042] of the Pre-Grant Pub. No. 20040038317, which states "[F]ragments less than 25 amino acids were considered non-viable." The same language can also be found in the '106 app. at page 16, lines 4-5. Similar supporting language can be found in the '339 App. at the bottom of page 3, continuing on to the top of page 4, which states "[F] or example, an enzyme (or subunit) of 500 amino acids (~60 kDa) has about 474 possible N-terminal fragments and a like number of possible C-terminal fragments, excluding the full-length molecule and assuming fragments of

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less than 25 amino acids are not viable." These passages each provide adequate support for the current amendment that the N-terminal fragment and the C-terminal fragment of the  $\beta$ -lactamase protein are not less than 25 amino acids in length.

Claim 63 is also amended to clarify that the first and second break-point are located "between 2 amino acid residues in a solvent exposed loop between Thr 195 and Ala 202." Support for the amendment can be found in the instant app. at page 6, paragraph [0042] and in the '106 app. at page 16, lines 10-13 which both state:

An exposed loop was identified by this method between two  $\alpha$ -helices of *E. coli* TEM-1  $\beta$ -lactamase (approximately Thr195 to Ala 202, between helices 7 and 8) within which the chain could be broken to produce fragments...

Similar support for a break-point in this solvent exposed loop is found in the '339 App. at page 12, Example 1, which states:

...the best performing pairs had more or less contiguous "new" termini (i.e., C-terminus of the  $\alpha$  and N-terminus of the  $\omega$  within ~5 residues), falling primarily within the loop between helices 7 and 8 (G196-T200, and not extending more than a few residues into either helix (L193-S203)).

Claim 66 is amended to recite that the location of the first and second break-point is between amino acid residues Glu 197 and Leu 198. Support for this amendment can be found in the instant application, for example, at page 6, paragraph [0042], and in the '106 app. at page 16, lines 14-22, which both state:

Representative fragments with contiguous break-point termini at Glu 197 and Leu 198 were designated  $\alpha$ 197 (N-terminal fragment) and  $\omega$ 198 (C-terminal fragment), and subsequently shown to produce selectable activity in the *E. coli* periplasm with interactions between a variety of heterologous domains fused to the break-point termini...

Similar support for the break-point between Glu 197 and Leu 198 can also be found in the '339 app. at page 12, Example 1, and in figure 5.

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The amendments to claims 72 and 74 merely clarify the claim language. New claims 75-77 merely recite combinations of enhancement tri-peptides previously recited in claim 74. Support for these enhancement tri-peptides can be found in the instant application at page 17, example 6, the table in paragraph [0097]; and in the '106 App. at page 46, example 6, lines 5-12. No new matter is added with the current amendments.

#### IV. PRIORITY

Examiner alleges that the filing date of the instant application is the actual filing date of September 22, 2003, because at least one or more of the following priority documents (09/526,106 ('106) filed March 15, 2000, 60/175,968 ('968) filed January 13, 2000; U.S. Prov. App. No. 60/135,926 ('926) filed May 25, 1999; U.S. Prov. App. No. 60/124,339 ('339) filed March 15, 1999, fail to provide adequate support under 35 U.S.C. §112, first paragraph for specific aspects of the claimed invention as detailed on page 3 of the Office Action. Specifically, with regard to claims 63, 66, 67, and 71-74, the Examiner alleges that none of the documents provide support for a genus of fragment complementation systems wherein "said first and second break-point termini are within 10 amino acids in either direction from a junction between 2 amino acid residues wherein said 2 amino acid residues are within a solvent exposed loop between elements of secondary structure." With regard to claims 68-70 and claims 72-74, the Examiner alleges that neither the '339 App. nor the '926 App. provide support for tri-peptides that enhance functional reconstitution. Applicants respectfully disagree.

As indicated *supra*, claim 63 as amended has specific expressed support in the instant application as filed, the '106 parent App., filed on March 15, 2000, and in the U.S. Prov. App ('339) filed March 15, 1999.

Independent claim 63, as presently amended, is adequately supported under 35 U.S.C. §112, first paragraph, as evidenced by the passages indicated above in Section III. The limitation that "said first and second break-point termini are within 10 amino acids in either direction from a junction between 2 amino acid residues" has been removed from the claim, rendering the objection to this limitation moot. With regard to the limitation that the break point

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is located within a solvent exposed loop, Applicants have amended the claim to recite a specific solvent exposed loop between amino acid residues Thr 195 and Ala 202. As indicated above in Section III, this limitation finds support in the instant App. at page 6, paragraph [0042] and in the '106 App. at page 16, lines 10-13, as well as in the '339 App. at page 12, example 1, as discussed *supra*. Applicants contend that claim 63 as presently recited is afforded priority to the '106 App. filed March 15, 2000 and to the '339 Prov. App. filed March 15, 1999. Because Claims 66, 67, and 71-74 depend either directly or indirectly from independent claim 63, the support identified for independent claim 63 is also applicable to the dependent claims.

In view of the above, Applicants respectfully request that the Examiner reconsider the priority claim for independent claim 63 and the claims that depend there from.

With regard to claims 68-70 and claims 72-74 the Examiner alleges that the specific tri-peptides that enhance functional reconstitution are not supported in either the '339 or the '926 application. Applicants respectfully disagree with the Examiner.

First, Applicants note that the enhancement tri-peptides are supported in the '106 application at example 6, page 46, lines 5-12, which provides expressed support for the tri-peptides HSE, NGR, GRE, EKR, REQ, QGN, DGR, GRR, and GNS. Moreover, this same table listing the same tri-peptides can also be found at page 17 of the priority application No. 60/175,968, filed January 13, 2000.

In view of the identified support as pointed to above, Applicants request that the Examiner acknowledge the status of the present application as a continuation of U.S. Pat. App. No. 09/526,106, ('106 app.) filed March 15, 2000, and claims benefit of U.S. Prov. App. No. 60/175,968 ('968 app.) filed January 13, 2000, and claims benefit of U.S. Prov. Pat. App. No. and claims benefit of U.S. Prov. App. No. 60/124,339 ('339 app.) filed March 15, 1999.

#### **V. REJECTIONS UNDER 35 U.S.C. §112, FIRST PARAGRAPH - NEW MATTER**

Claims 63, 66, 67, and 71-74 stand rejected under 35 U.S.C. §112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to a skilled artisan that the inventor was in possession of the invention as presently claimed at the time the application was filed. This rejection is essentially maintained

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from the previous Office Action mailed January 5, 2007, with the added rejection directed to the phrase "at least 25 amino acids in length." Applicants respectfully traverse the rejection, to the extent that it applies to the claims as presently amended.

The claims as presently amended recite that the break-point is between 2 amino acid residues within the solvent exposed loop between amino acid residues Thr 195 to Ala 202. The claims as presently recited do not read upon any solvent exposed loop, nor do the claims read upon break-points in different solvent exposed loops. Furthermore, the Examiner has acknowledged that the inventors were in possession of a break-point in this solvent exposed loop (Thr 195 to Ala 202), stating "thus it would appear that only one loop (*i.e.* Thr195 to Ala202) was identified...." *See*, page 6 of the Final Office Action mailed July 30, 2007.

The Examiner alleges that the phrase "at least 25 amino acids in length" is not supported because there is no upper limit as to the length. Applicants respectfully disagree with the Examiner. A skilled artisan reading the application as filed, would understand that while fragments less than 25 amino acids in length are not viable, a fragment at least 25 amino acids in length, while viable, would have an upper size limit being 25 amino acids less than the full length of the protein. However, in an effort to expedite allowance of the application, Applicants have amended the claim language to clarify that the fragments are not less than 25 amino acids in length. This is consistent with the express language in the specification, which states that "fragments less than 25 amino acids were considered non-viable."

In view of claims as presently amended and the arguments presented above, Applicants request that the Examiner withdraw the rejection.

#### **VI. REJECTIONS UNDER 35 U.S.C. §102**

The Examiner has maintained the rejection that claims 63, 66, 67, 71 and 72 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Wehrman *et al.* PNAS March 19, 2002, 99(6):3469-3474. Specifically the Examiner has maintained the rejection on the grounds that the Applicants were not afforded the priority date of at least one of the earlier application (*i.e.* U.S. pat. App. No. 09/526,106, filed March 15, 2000). Applicants traverse the rejection.

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The claims as presently amended are supported by at least the ('106 app.) as indicated above in the sections for claim support and priority. Wehrman *et al.* is not prior art to the claims as presently recited because each of the claim elements disclosed by Wehrman *et al.* is disclosed in at least the parent application 09/526,106, filed March 15, 2000, which is nearly 2 years prior to the March 19, 2002 publication date of Wehrman *et al.* Because Wehrman *et al.* is not prior art to the presently claimed invention, Wehrman *et al.* cannot anticipate the claimed invention.

#### VII. REJECTIONS UNDER 35 U.S.C. §102/103

The Examiner has maintained the rejection of claims 63, 66, 67, and 71 under 35 U.S.C. §102(e) as allegedly being anticipated or in the alternative under 35 U.S.C. §103(a) as allegedly being unpatentable over Michnick *et al.* (U.S. Pat. No. 6,828,099) filed May 31, 2001, alone or in view of Galameau *et al.* *Nat. Biotech* 2002 20:619-622, as evidenced by Applicants Exhibit 1 filed October 26, 2006. Applicants disagree.

As indicated above, the claims as presently recited are supported by the priority documents, specifically, U.S. Pat. App. No. 09/526,106, filed March 15, 2000, U.S. Prov. App. No. 60/175,968, filed January 13, 2000, and U.S. Prov. App. No. 60/124,339, filed March 15, 1999. Each of these applications is at least 1 year prior to the priority date of Michnick *et al.*, and at least two years prior to the publication date of Galameau *et al.* Therefore, the cited references are not prior art to the presently claimed invention. Because the cited references are not prior art, the cited references cannot anticipate the invention as presently claimed.

#### VIII. REJECTION UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 63, 66, and 71-74 stand rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. Specifically, the Examiner alleges that the phrase "the direction of translation" in claim 63 lacks antecedent basis. Applicants disagree.

The phrase "the direction of translation" in claim 63 does not require antecedent basis because there is only a single direction of translation. The phrase was added to the claim to

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indicate the order of the components in the first and second oligopeptides comprising the fragment complementation system.

In view of the above, Applicants respectfully request that the Examiner withdraw the rejection.

**CONCLUSION**

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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